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211 (b) Research Group

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NON-CONFIDENTIAL INFORMATION

January 15, 2002

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(ATTN: Section 8(e) Coordinator)
Office of Toxic Substances
U.S. Environmental Protection Agency
401 M Street, SW
Washington, DC 20460

Contain NO CBI

2002 MAR -5 PM 12:17

Re: TSCA (8e) Submission for Clean Air Act Section 211(b) Gasoline/ETBE Vapor Condensate (Lot # API 01-05)

Dear Sir/Madam:

The 211(b) Research Group (see attached membership list) is an unincorporated group of US fuel and fuel additive manufacturers affiliated by contractual obligation to meet the testing requirements of Section 211(b)(2) and 211(e) of the Clean Air Act. The 211(b) Research Group, on behalf of its member companies, is submitting this notice pursuant to TSCA Section 8(e). This notice is based on preliminary results from a study to evaluate immune system function after exposure to vapors of unleaded gasoline blended with gasoline/ethyl tertiary butyl ether (ETBE). The study found that 4-weeks of exposure significantly suppressed immune system function in rats.

As part of the 211(b) Alternative Tier II test program on gasoline (CAS No. 86290-81-5) containing 17% ETBE (CAS No. 637-92-3), a plaque forming cell assay study was performed on spleen cells from rats (10 females/group) exposed to gasoline/ETBE vapor (13.5% ETBE) by inhalation at concentrations of 0, 2000, 10,000 and 20,000 mg/m^3, 6 hr/day, 5 days/week for 4 weeks. The positive control compound was cyclophosphamide (50mg/kg) administered intraperitoneally once per day for four days prior to spleen collection. Four days prior to spleen collection, the animals were immunized by i.v. injection with 2x10^8 sheep red blood cells (sRBC). Spleens were prepared into single cell suspensions and the number of IgM sRBC antibody-forming cells (AFC) was determined

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Statistical evaluation of unaudited data, using one-way analysis of variance followed by Dunnett's t Test, showed statistically significant ($p \leq 0.01$) decreases in AFC in the mid and high dose groups relative to the control group. (Summary tables attached).

Decreased AFC response indicates that the test material is capable of modifying the humoral immune response in the whole animal. However, the significance of these results for potential human health hazard assessment is unknown at this time.

Preliminary results from a similar study with unoxygenated gasoline vapor in rats were negative.

When the final report of the Plaque Forming Cell Assay study is complete, it will be submitted to the EPA Office of Transportation and Air Quality, Fuels and Energy Division, as part of the requirements of Clean Air Act Section 211(b)(2) and 211(e) (Docket No. A-90-07). If you require further information, please contact Lorraine Twerdok at 202-682-8344, or by mail at this address.

Regards,

Lorraine E. Twerdok

Lorraine Twerdok, Ph.D., DABT
Administrator, 211(b) Research Group

Cc: John Brophy, EPA
Mike Davis, EPA
Tom Goldsworthy, ILS
Rich Schlesinger, NYU
211(b) Research Group Member Companies

Table

Spleen Antibody-Forming Cell Response to T-dependent Antigen Sheep Erythrocytes in Female Sprague Dawley Rats Exposed to Gasoline ETBE Vapor Condensate via Inhalation for 5 Days per Week for 4 Weeks

Day 4 Response
HLS Study No. 00-6129

Exposure	Body Wgt (g)	Spleen Wgt (mg)	Spleen Cells ($x10^7$)	IgM AFC/ 10^6 Spleen Cells	IgM AFC/Spleen ($x\ 10^3$)
Vehicle	259.0 ± 5.0 (10)	597 ± 37 (10)	71.48 ± 4.48 (10)	556 ± 76 (10)	391 ± 48 (10)
Gasoline ETBE Vapor Condensate					
2000 mg/m^3	263.0 ± 3.2 (10)	608 ± 41 (10)	74.21 ± 3.69 (10)	576 ± 94 (10)	427 ± 72 (10)
10000 mg/m^3	259.4 ± 4.0 (10)	608 ± 25 (10)	72.95 ± 1.27 (10)	136 ± 23** (10)	100 ± 17** (10)
20000 mg/m^3	250.3 ± 3.5 (10)	603 ± 17 (10)	72.34 ± 2.78 (10)	153 ± 39** (10)	117 ± 35** (10)
Cyclophosphamide 50 mg/kg	247.0 ± 4.0 (10)	299 ± 17** (10)	15.79 ± 1.21** (10)	0 ± 0** (10)	0 ± 0** (10)
H/NH	H	H	NH	NH	NH
Trend Analysis	NS	NS	NS	$p \leq 0.01$	$p \leq 0.01$

Female Sprague Dawley rats were administered vehicle control (air only) or gasoline ETBE vapor condensate by inhalation via whole-body exposure for 5 days per week for 4 weeks. The positive control, cyclophosphamide, was administered i.p. the last 4 days of exposure. Four days prior to sacrifice, the rats were immunized (iv) with $2x10^8$ sRBC. On the day of sacrifice, spleens were placed in tubes containing media and sent to Richmond, VA, on ice for next day cell preparation. Spleens were prepared into single cell suspensions and the number of IgM sRBC antibody-forming cells was determined. Values represent the mean ± SE derived from the number of animals indicated in parentheses. H = homogeneous data and NH = non-homogeneous data using the Bartlett's Test for homogeneity. Homogeneous data were evaluated using a parametric analysis of variance. When significant differences occurred, exposed groups were compared to the vehicle control group using the Dunnett's t Test. Non-homogeneous data were evaluated using a non-parametric analysis of variance. When significant differences occurred, exposed groups were compared to the vehicle control group using the Wilcoxon Rank Test. The positive control was compared to the vehicle control using the Student's t Test. Values significantly different from vehicle control at $p \leq 0.05$ are indicated by an asterisk, while those significant at $p \leq 0.01$ are noted by a double asterisk. The Jonckheere's Test was used to test for dose-related trends among the vehicle and exposed groups.

Table

Body Weight (g) and Organ Weights (mg) in Female Sprague Dawley Rats Exposed to Gasoline ETBE Vapor Condensate via Inhalation for 5 Days per Week for 4 Weeks

HLS Study No. 00-8129

Parameter	Vehicle (10)	Gasoline ETBE Vapor (mg/m³) 2000 (10)	10000 (10)	20000 (10)	Cyclophosphamide 50 mg/kg (10)	H/NH	Trend Analysis
Body Wgt (g)	259.0 ± 5.0	263.0 ± 3.2	259.4 ± 4.0	250.3 ± 3.5	247.0 ± 4.0	H	NS
Spleen (mg)	597 ± 37	608 ± 41	608 ± 25	603 ± 17	299 ± 17**	H	NS
% Body Wgt	0.230 ± 0.011	0.230 ± 0.014	0.235 ± 0.012	0.240 ± 0.006	0.120 ± 0.006**	H	NS
Thymus (mg)	593 ± 45	549 ± 31	579 ± 40	605 ± 48	123 ± 9**	H	NS
% Body Wgt	0.228 ± 0.016	0.209 ± 0.013	0.220 ± 0.013	0.241 ± 0.018	0.049 ± 0.004**	H	NS

Female Sprague Dawley rats were administered vehicle control (air only) or gasoline ETBE vapor condensate by inhalation via whole-body exposure for 5 days per week for 4 weeks. The positive control, cyclophosphamide, was administered i.p. on the last 4 days of exposure. On the day of sacrifice, spleens were placed in tubes containing media and sent to Richmond, VA, on ice for next day cell preparation. The rats were necropsied and indicated organs weighed. Values represent the mean ± SE derived from the number of animals indicated in parentheses. H = homogeneous data and NH = non-homogeneous data using the Bartlett's Test for homogeneity. Homogeneous data were evaluated using a parametric analysis of variance. When significant differences occurred, exposed groups were compared to the vehicle control group using the Dunnett's t Test. The positive control was compared to the vehicle control using the Student's t Test. Values significantly different from vehicle control at $p \leq 0.05$ are indicated by an asterisk, while those significant at $p \leq 0.01$ are noted by a double asterisk. The Jonckheere's Test was used to test for dose-related trends among the vehicle and exposed groups.

SECTION 211(b) RESEARCH GROUP MEMBERSHIP
YEAR 2002

Organization
3M Automotive Aftermarket Division
A.E. Staley Manufacturing Company
Aectra Refining & Marketing
AGP Corn Processing
Akzo Nobel Chemicals Inc.
Albemarle Corporation
Amerada Hess Corporation
ANGUS Chemical Co. a subsidiary of Dow Chem. Co.
Archer Daniels Midland Company
Astra Oil Company, Inc.
ATOFINA Oil and Chemical Company
Baker Petrolite
BASF Corporation
Bayer Corporation *(new member)*
Belvieu Environmental Fuels/Enterprise Products
Betz Process Chemicals
Big West Oil/Flying J Inc.
Blue Coral Inc.-Slick 50 Products Corp.
BP p.l.c. [BP, AMOCO, ARCO]
Buckeye Refining Co. LLC (was American Rfg Group)
Buckman Laboratories, Inc.
Calcasieu Refining Company
Calumet Lubricants (own Pennzoil's Rouseville Refinery)
Castrol North America Holdings Inc.

Cenex Inc.
Champion Technologies, Inc.
Chevron Products Company
Chief Ethanol Fuels Inc.
CITGO Petroleum Corporation
Coastal States Management
Conoco, Inc.
Countrymark Cooperative, Inc.
CRC Industries, Inc./K&W Products
Crompton Corp. (was Witco Corp.)
Crown Central Petroleum Corp.
Ecofuel S.p.A. (American AGIP)
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Eott Energy Operating LTD Partnership
Equistar Chemicals/Lyondell Chem. Co.
Equiva Services LLC [and Texaco]
Ergon, Inc.
Ethyl Corporation
ExxonMobil Biomedical. Sciences. Inc. (*was Mobil Corp*)
ExxonMobil Refining & Supply Company
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Farstad Oil, Inc.
First Brands Corporation
Fortum Oil and Gas (was Neste Oy)
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Giant Industries Arizona, Inc.
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Grain Processing Corporation
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Guardsman Products/Valspar
Gulf Oil Limited Partnership
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Hunt Refining Company
Huntsman Corporation
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Irving Oil Transportation Company
Kern Oil & Refining Company
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Kinder MorganEnergy Partners/Kinder Morgan Operating LP "A"
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Kop-Coat, Inc./Valvtect Petroleum/Alox Chem**
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Lyondell-CITGO Refining LP
Marathon Ashland Petroleum LLC (MAPLLC)
Mid-America Dairymen, Inc./Golden Cheese Co. of California
Midwest Grain Products, Inc.
Minnesota Corn Processing
Murphy Oil Corporation

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Nalco Chemical Company/Exxon Energy Chemicals, LP
National Cooperative Refining Association/Cooperative Refining, LLC
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New Energy Corp.
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Octel America, Inc.
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Sabic Americas, Inc.
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Organization
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Western Petroleum Company
Williams Refining, LLC (was Mapco, Inc.)
Wynnewood Refining Company
Wyoming Refining Company